

# A pilot study to determine whether external stabilisation of the chest wall reduces the need for mechanical ventilation in preterm infants

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**Objectives.** This was a pilot study to determine whether external stabilisation of the chest wall with a splint reduces the need for mechanical ventilation in preterm infants, within the first 7 days after study entry.

**Design.** This was a non-blinded prospective randomised controlled study. After consent was obtained, babies were randomised into a chest splint or control group.

**Setting and time.** The study was conducted in the neonatal units of Johannesburg and Chris Hani Baragwanath hospitals between January 2004 and December 2005.

**Subjects.** Preterm infants with a birth weight above 1 000 g with respiratory distress syndrome requiring more than 25% supplemental oxygen to maintain oxygen saturation above 90% during the first day of life.

**Outcome measures.** The primary outcome measure was the need for mechanical ventilation within 7 days of study entry; secondary outcome measures were survival at 30 days, air leak and intraventricular haemorrhage.

**Results.** There were 40 infants enrolled, 19 randomised to the chest splint group and 21 to the control group. Demographic characteristics were comparable, although the splint group required significantly more supplemental oxygen at enrolment. Four of the 19 infants in the splint group and 5 of the 21 controls required mechanical ventilation (not significant). There was no air leak in any of the study subjects during the study period. Twelve infants in each group had cranial ultrasound scans: there was one grade 3 intraventricular haemorrhage, one periventricular echodensity and one germinal matrix cyst in each group. Three of the 21 controls and 2 of the 19 splint group infants died within the first 30 days; no death was related to the chest splint. There were no local complications related to the chest splint, such as skin rash or pressure sores.

**Conclusion.** This small study did not demonstrate any reduction in the need for ventilation with the use of the chest splint. Use of the splint was not associated with any complications and therefore appears to be safe to use. Further studies with larger numbers are warranted.

Respiratory distress syndrome (RDS), caused by surfactant deficiency, is a common cause of respiratory failure in preterm infants. RDS is treated by administration of exogenous surfactant and ventilatory support as needed, in the form of intermittent positive-pressure ventilation (IPPV) or continuous distending pressure (CDP). Bronchopulmonary dysplasia (BPD) remains a problem, despite improvements in the technique of conventional positive-pressure ventilation, so non-invasive forms of ventilation such as nasal continuous positive airways pressure (NCPAP) are of interest.<sup>1</sup> NCPAP together with permissive hypercapnia appears to decrease the incidence of BPD significantly.<sup>2</sup> NCPAP is currently widely used in the management of RDS in preterm infants.<sup>2-5</sup> Surfactant therapy with early extubation to NCPAP decreases the need for intubation and ventilation,<sup>6-8</sup> shortens the duration of mechanical ventilation, decreases the need for subsequent surfactant therapy<sup>9</sup> and decreases BPD in extremely low-birth-

weight (ELBW) infants. Whether NCPAP should be started immediately at birth or delayed until the baby has signs of RDS is still unclear<sup>10-13</sup> and is currently under evaluation.<sup>14</sup> The application of NCPAP immediately after birth may reduce the need for subsequent surfactant therapy.<sup>13</sup> NCPAP is also useful in facilitating extubation and managing the apnoea of prematurity. While highly effective, NCPAP is not always successful<sup>15</sup> and may be associated with complications such as pneumothorax,<sup>13</sup> a greater risk of early-onset sepsis in ELBW infants<sup>16</sup> and the development of nasal trauma.<sup>17,18</sup>

Continuous negative airways pressure (CNEP) is another way of delivering CDP. CNEP was found to be physiologically equivalent to positive end-expiratory pressure (PEEP) in an animal model of acute lung injury<sup>19</sup> and is effective in the management of RDS in preterm infants.<sup>20,21</sup> However, while NCPAP has gained favour, CNEP has remained largely un-utilised. The systems used to apply CNEP are often

cumbersome, e.g. custom-made incubators,<sup>22</sup> while NCPAP is simpler to apply and allows better patient access.<sup>20</sup> A trial in the management of RDS in neonates using CNEP<sup>22</sup> showed a reduction in the need for intubation and duration of oxygen therapy. There was a trend towards an increase in mortality and cranial ultrasound abnormality in the CNEP group, which was reported as not significant. The trial and reported complications generated a great deal of publicity and accusations of research fraud.<sup>23,24</sup> Although long-term follow-up has shown that the CNEP group of infants did not suffer from any long-term detrimental effect, respiratory or neurological,<sup>25</sup> the controversy generated may have contributed to the failure of CNEP to gain popularity as a therapy. There are only limited data on the use of CNEP in paediatric (not neonatal) patients, particularly in the use of a cuirass after cardiac surgery.<sup>26</sup> A Cochrane review comparing CNEP and CPAP in paediatric patients, which includes one small study,<sup>27</sup> concludes that there is a lack of well-designed trials evaluating the benefit of non-invasive ventilation in paediatric patients.

The chest splint (Hug 'n Snug<sup>TM</sup> Neonatal Chest Splint, Respironics, Murrysville, PA) is a newly developed device that is still under evaluation. The splint is designed to provide CNEP to neonates with RDS. It is a firm plastic device that is applied to the chest wall using two adhesive chest plates (front and back plates) (Fig. 1). In infants with RDS the atelectatic lungs cause the compliant chest wall to collapse inwards in the anteroposterior (AP) dimension.<sup>28</sup> The splint prevents chest wall retraction and is adjustable in the AP dimension. This allows for correction of any chest wall flattening. A small preliminary trial showed that the splint maintains chest expansion and improves functional residual capacity and tidal volume in spontaneously breathing neonates.<sup>29</sup> It does this by producing negative distending pressure and making spontaneous breathing efforts more effective. Small pilot studies have shown that oxygenation improves, retractions can be eliminated, and there is an improvement in blood pressure.<sup>30,31</sup>



**Fig. 1. Neonatal chest splint.**

Supplemental oxygen is administered either by nasal cannulae or via head box. If the splint performs as expected, it may potentially provide a non-invasive form of ventilatory support via negative extrathoracic pressure. The baby may not require intubation, and this could potentially be of great advantage where access to ventilatory support is limited.

## Aims

This was a pilot study to evaluate the effect of an external chest splint (Hug 'n Snug<sup>TM</sup>) in the management of RDS in neonates. The primary objective was to determine whether the chest splint reduced the need for mechanical ventilation within the first 7 days after entry into the study in preterm infants with RDS. The secondary objective was to evaluate potential complications of the splint, particularly increased blood pressure, air leak and intraventricular haemorrhage, as well as survival at 30 days.

## Subjects and methods

This was a non-blinded prospective randomised controlled trial conducted in the neonatal units of Chris Hani Baragwanath and Johannesburg hospitals between January 2004 and December 2005. Eligible infants were preterm infants (<37 completed weeks' gestation) with a birth weight above 1 000 g during the first 24 hours after delivery.

### Inclusion criteria

Eligible subjects were spontaneously breathing infants with clinical evidence of RDS, including tachypnoea and chest wall retractions, requiring >25% supplemental oxygen to maintain saturations between 90% and 95% with radiological evidence of RDS (ground glass appearance and air bronchograms), within 24 hours of birth.

### Exclusion criteria

Babies with the following conditions were excluded from the study: artificial airway, receiving mechanical ventilation or CPAP, primary diagnosis of a cardiac abnormality with right-to-left shunting, air leak, meconium aspiration syndromes, malformations of the chest wall unrelated to reversible lung disease, post surgery, respiratory failure (supplemental oxygen >65% to maintain saturations above 90%, pH <7.25 with arterial PCO<sub>2</sub> 60 mmHg or recurrent intractable apnoea producing oxygen saturations below 70% with a heart rate below 80 beats/min), any contraindication to ventilation as per intensive care unit policy (including birth weight <1 000 g, severe birth asphyxia and major congenital abnormalities with a poor long-term outcome).

Delivery room care at the time of the study included resuscitation with bag and mask as required and intubation for apnoea or severe asphyxia. Babies that did not need immediate mechanical ventilation were given supplemental oxygen via headbox. NCPAP was not available in the delivery suite and surfactant was only administered to babies requiring mechanical ventilation as rescue therapy.

Once informed consent was obtained, babies were randomised by means of sequentially numbered sealed envelopes into control (standard care) or splint groups. Standard care consisted of supplementary oxygen via head box, intravenous fluids, maintenance of temperature, oral feeds and antibiotic therapy as required. The chest splint group received standard care plus placement of the chest splint. NCPAP was not available in the unit at the time. Surfactant therapy was only administered to those babies who needed intubation and mechanical ventilation, so no baby received surfactant while

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taking part in the study. The study was only conducted during the day on weekdays in order to allow the same trained researcher to apply and remove the chest splint, thereby minimising the influence of staff variation.

### Chest splint

The chest splint (Hug 'n Snug™ Neonatal Chest Splint, Respironics) is a firm plastic device (Fig. 1) applied to the chest by means of a moulded plastic front and back plate, and fixed to the skin with hydrogel. The front and back halves of the splints can readily expand but are not collapsible and hence prevent sternal retraction. The plates and splint come in different sizes and the degree of expansion of the splint is adjustable on the sides of the splint. The front plate should fit comfortably over the sternum and extend to the costochondral junctions, without extending onto the abdomen. The infant's chest is measured using calipers and the thoracic index (TI) calculated (AP over lateral dimensions). The correct size of splint and degree of expansion can be determined from standard tables.<sup>29</sup> Gradual expansion of the splint in the AP diameter can restore the collapsed ribcage to normal dimension via an outward pulling force (negative distending pressure) applied to the chest wall. The mattress that the baby lies on has a groove in it to allow space for the chest splint, thereby preventing pressure sores. The splint was removed and changed daily by research staff. The TI was measured and the splint was adjusted according to the new measurements and reapplied. The TI was determined daily in the control group.

All other care was provided by attending staff according to standard protocols. Supplemental oxygen was weaned if the oxygen saturations were more than 90%. The endpoint of the study was respiratory failure (as defined above), supplemental oxygen less than 25% or 7 days after entry into the study. Respiratory rate, heart rate, blood pressure and oxygen saturations were measured at enrolment, hourly for 4 hours thereafter and then 3-hourly until the infant's supplemental oxygen requirement was below 25%. It was not considered ethically justified to subject study babies to repeated arterial blood gas analysis, as this was not routine care in the unit. If at any point the baby developed respiratory failure, the chest splint was removed and the baby was intubated and transferred to the intensive care unit for ventilation. This decision was made in consultation with research staff. All babies were scheduled to have a cranial ultrasound scan within the first week of life and then before discharge. Study patients were monitored until discharge from hospital and complications were noted.

The study was approved by the human research ethics committee of the University of the Witwatersrand. Informed consent was obtained from parents before enrolment.

## Statistical methods

### Sample size

This was a pilot study. There were limited clinical data available on the potential magnitude of benefit of the chest splint and the number of infants meeting the entry criteria for the study



*There were no serious complications related to use of the splint in this small study.*

who would ultimately require ventilation was not firmly established. A sample size of 30 patients per group was therefore proposed as an initial sample for a pilot study. The data obtained would then allow for further studies to be planned.

### Data analysis

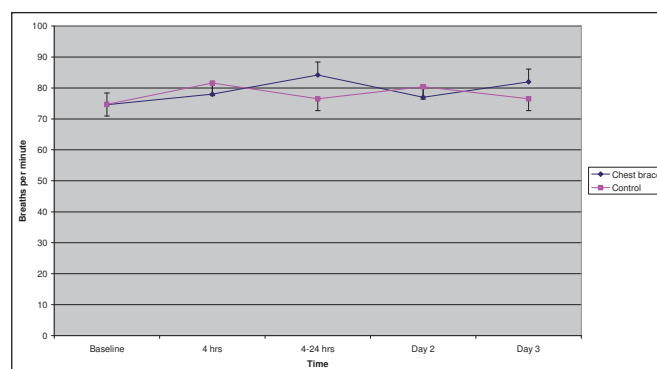
The data were analysed using standard statistical methods on Microsoft Excel version 2003. Continuous variables were described as mean and standard deviation (SD), with categorical variables as percentages. Continuous variables had a normal distribution, so comparison was done by way of unpaired *t*-tests, with a significance level of  $p < 0.05$  (two-tailed). Categorical variables were compared by means of Fisher's exact test. Observations (respiratory rate, mean blood pressure,

supplemental oxygen) were done at baseline, hourly for the first 4 hours and then 3-hourly until study completion. The highest mean blood pressure, highest respiratory rate and lowest fraction of inspired oxygen to maintain saturations above 90% were established and compared for the following time periods: baseline, the next 4 hours, the following 16 hours (4 - 24 hours) and then daily until study completion (time periods 0, 1, 2, 3, 4).

## Results

One hundred and forty babies were screened for entry into the study - 38 had respiratory failure, 42 did not have significant RDS and had no need for supplementary oxygen, consent was not obtained for 6, 7 had a birth weight just below 1 000 g, 2 were above 36 weeks' gestation, and 8 were excluded for miscellaneous reasons. During early 2005, NCPAP and surfactant became available in level 2 care and the rate of enrolment into the study declined significantly, so the study was stopped in December 2005.

Forty babies were therefore entered into the study, 19 in the chest splint group and 21 in the control group (Table I). Six of the babies were from Chris Hani Baragwanath Hospital and the remainder from Johannesburg Hospital. There were no significant differences in demographic characteristics between the groups. The baseline TI was similar in the two groups (73.3% v. 72.6%, not significant). Baseline blood pressure and respiratory rate were the same, but the splint group had a significantly higher level of supplemental oxygen at the start. Blood pressure, respiratory rate, supplemental oxygen requirement and TI are shown in Figs 2 - 5.



**Fig. 2. Respiratory rate.** *There were no significant differences in respiratory rate between the chest splint and control groups.*



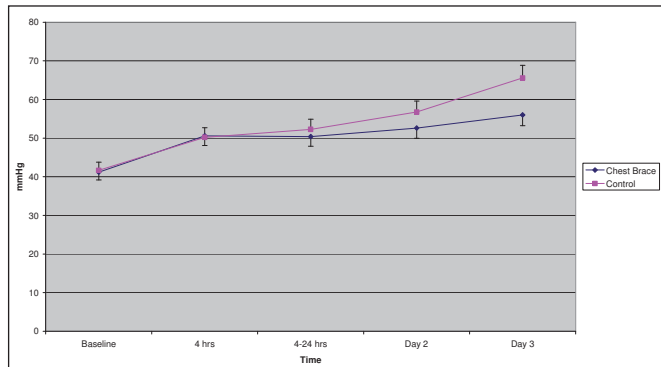


Fig. 3. Mean blood pressure. There were no significant differences in mean blood pressure between the chest splint and control groups.

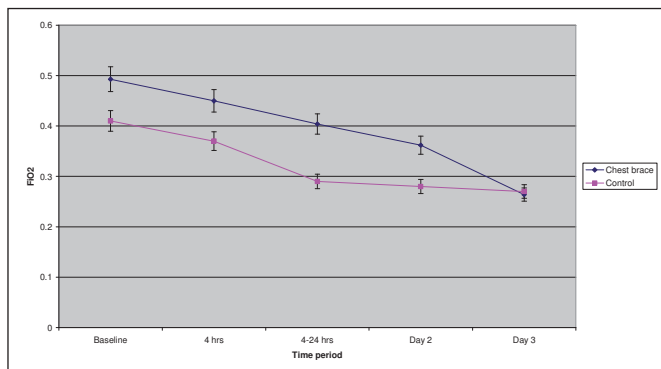


Fig. 4. Oxygen requirement. p-values – baseline 0.068; 4 hours 0.08; 4 - 24 hours 0.02 (significantly different); day 2, 0.275; day 3, 0.87.

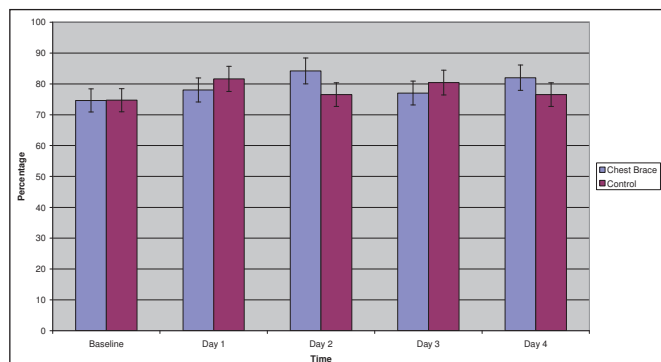


Fig. 5. Thoracic index (TI). There were no significant differences in TI between the control and chest splint groups.

The outcomes of the two groups were comparable; in particular, the need for ventilation was the same. Nine babies (5 control group, 4 splint group) were ventilated during the study period, 8 within the first 48 hours after study entry. One control subject was ventilated on the 6th day of the study. The most common indication for ventilation was hypoxaemia

(4 control group, 3 splint group). No baby in either group had any form of air leak during the study period. One baby in the chest splint group was discharged home on oxygen as opposed to none in the control group. Owing to technical problems with the cranial ultrasound machine during the study period, only 12 babies in each group had cranial ultrasound scans; 1 grade 3 intraventricular haemorrhage, 1 periventricular echodensity and 1 germinal matrix cyst was found in each group. There were no skin rashes or pressure sores related to the chest splint. There were 5 deaths, 2 in the splint group (1 at 30 days from septicaemia and 1 at 11 days from probable sepsis) and 3 in the control group (1 at 5 days from pulmonary haemorrhage, 1 at 14 days from necrotising enterocolitis, and 1 at 15 days, related to neonatal transport). None of the deaths was related to the chest splint.

## Discussion and conclusion

CNEP is a non-invasive means of providing ventilatory support to preterm infants with RDS.<sup>20,21</sup> The Hug 'n Snug chest splint may provide a simple means of providing CNEP to these patients, which could potentially be of great benefit in low-resourced settings. The chest splint is still under evaluation, and there are not a lot of clinical data to support this hypothesis. This was a small pilot study to determine whether the splint could reduce the need for mechanical ventilation in the first week of life in preterm infants with RDS. The splint is straightforward to apply once the technique has been learned. Attention must be paid to the correct sizing of the splint and its adjustment according to the TI. There were no major technical problems relating to the splint in this small study.

The study failed to show any benefit from the splint. There are several possible reasons for this, including:

- Small sample size.
- Application of the splint after some hours; it may be more effective to apply the splint immediately after birth to prevent worsening atelectasis.
- Lack of surfactant administration – surfactant therapy before application of the splint may show similar benefits to the use of surfactant with NCPAP.
- Exclusion of babies <1 000 g – the splint may benefit ELBW infants, who are at greater risk of RDS and often have sternal recession.
- Enrolment of relatively well babies – mean supplemental oxygen was below 50% in both groups, so the majority of these infants did not require ventilatory support.
- The treatment group had a greater need for supplemental oxygen at the time of enrolment, which may indicate that they were sicker babies and could have masked a potential benefit from the splint.

TABLE I. DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF THE STUDY SUBJECTS

Characteristic	Control	Splint	p-value
Gestational age (wks) (mean (SD))	30.47 (2.4)	31.26 (2.8)	0.34
Weight (g) (mean (SD))	1 393 (352)	1 522 (447)	0.31
Females/males	11:10	10:9	0.98
Deaths (No.)	3	2	0.55
Thoracic index (TI) at baseline (%) (mean (SD))	72.2 (3.6)	72.98 (6.41)	0.41
FIO <sub>2</sub> at baseline (mean (SD))	0.49 (0.11)	0.41 (0.11)	0.068
Mean blood pressure (mmHg) at baseline (mean (SD))	41.56 (4.57)	41.3 (7.48)	0.90
Respiratory rate at baseline breaths/min (mean (SD))	74.7 (15.7)	74.45 (18.3)	0.96

- The age and weight range of the infants enrolled was wide, resulting in a non-homogeneous group; it would have been preferable to investigate the use of the chest splint in VLBW or ELBW preterm infants.
- The splint would be expected to be most effective in those infants with greatest sternal recession. This would correspond to a TI below 72%. A low TI was not a criterion for inclusion in the study.

There were no serious complications related to the use of the splint in this small study, suggesting that it is safe to use in a clinical setting. We would therefore recommend further clinical trials on the use of the splint, taking note of the possible reasons for failure of this pilot study. The splint could also be considered for use in facilitating extubation in preterm infants. We speculate that the application of the front chest plate alone is a very simple measure that may reduce sternal retraction and improve the efficiency of breathing in the most vulnerable ELBW infants, but this needs further evaluation.

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